REMARKS

Claims 1, 4-6, and 9-47 are currently pending is this application. Claims 11-22, 25-34, and 38-47 have been withdrawn due to restriction requirement. Claims 2, 3, 7, and 8 have been canceled. Claim 1 has been amended to include the subject matter of canceled claims 3and 8. Claim 4 has been amended to provide proper antecedent basis. No new matter has been added.

Applicants acknowledge and appreciate the fruitful discussion between the undersigned attorney and Examiner Ghali on May 1, 2011. Examiner Ghali agreed to reconsider Applicants request to disqualify the Adusimilli reference based upon 35 USC 103(c) and to re-open prosecution.

Specification

The Examiner acknowledges the amendment made to the specification. However, the Examiner noted that "Eudragit NE 30" has been replaced by "EUDRAGIT® NE", and it is not clear to the Examiner if "NE 30" and "NE" are the same trademarks having the same composition. Applicants have corrected this typographical error.

Claim Rejections -35 USC 3 103

Claims 1-10, 23-24, 35-37 are rejected under 35 U.S.C. 103(a) as allegedly being obvious over Chen et al. (US 2003/0068376) in view of Lerner et al. (US 6,197,331), as evident by the article by Lamosa et al. ("Design of Microencapsulated Chitosan Microspheres for Colonic Drug Delivery"). Applicants traverse this rejection.

One-skilled in the art would not combine the cited references. Chen is directed to "an intraoral ***quick-dissolving film*** which is applied lingually. The dosage form is applied to the tongue . . . and rapidly disintegrates, dissolves and releases [nicotine]." (Chen, paragraph [0051]) (emphasis added). As recognized by the Action, Chen does not teach the use of enteric polymers for its film. Rather, the films in Chen comprise a non-microbial hydrocolloid and nicotine. Chen describes this non-microbial hydrocolloid as water soluble and non-gelling natural gums or derivatives thereof, water soluble and non-gelling polypeptides, and water soluble synthetic polysaccharides. There is no suggestion in Chen that these water soluble components can or should be replaced with enteric polymers or that enteric polymers would produce the described quick-dissolving film. The quick-dissolving film of Chen provides for "a relatively rapid initial increase in blood nicotine concentration

[that] simulate[s] the pattern obtained by smoking a cigarette or taking a nasal spray." (Chen, paragraph [0052]).

Lerner is directed to an oral patch that "adhere[s] to hard dental surfaces, such as teeth and dentures." (Lerner, col. 1, lines 11-12) (emphasis added). The oral patch is designed to ***remain on the tooth*** or denture for a period of time and provide ***controlled or sustained release*** of pharmaceutical agents to the patent. Although Lerner refers to certain enteric Eudragit® polymers[1] as suitable polymers for release layers and/or adhesive layers, there is no discussion of these polymers imparting "quick dissolving" characteristics on the oral patch. This lack of teaching is consistent with the understanding of one skilled in the art with respect to enteric coatings – enteric polymers are useful for delayed release of an active agent until a particular dosage form reaches the intestine. Lerner repeatedly refers to controlled or sustained release characteristics of the oral patch. This is consistent with Lerner's use of the enteric polymers to enhance mucoadhesion to immobilize the device in the oral cavity and regulate its release mechanisms, such as erosion and diffusion, for a prolonged period of time. Additionally, Lerner further distinguishes itself from quick dissolving films, like those disclosed in Chen. Lerner states that a significant advantage of its "oral patch" over films is that the oral patch provides for greater adhesion than films, resulting in ***treatment for longer periods of time*** (Lerner, col. 10, lines 17-26).

Additionally, there is no suggestion or motivation to combine Chen with Lerner because combination of these references would result in a nicotine film that would be unsatisfactory for its intended purpose. Indeed, combination of the nicotine salts disclosed in Chen with the enteric polymers disclosed in Lerner would not result in a film that would dissolve in the oral cavity to release nicotine completely. The nicotine disclosed in Chen is limited to "nicotine base and its salts." The enteric polymers recited in Lerner require a specific pH to be soluble. For example, Eudragit L100 will only dissolve at a pH above 5.5. If one were to combine the nicotine salts disclosed in Chen with these polymers directly, the acidic counter ions associated with the nicotine salts would lower the pH of the formulation and not provide the critical pH needed to dissolve the film. This makes it inoperable for its intended purpose which is to release nicotine rapidly into the oral cavity of a user when administered on the tongue.

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[1] Contrary to the Action's statement that "applicants themselves admit, Lerner teaches neutral enteric polymers" 2/8/2011 Action, page 17), Applications do not admit that Lerner teaches neutral enteric polymers.

Furthermore, even if one were motivated to combine the references, combination of these references does not teach the claimed invention. Independent claim 1 has been amended to recite a ***nicotine oil***. As recognized by the Examiner, Chen does not disclose nicotine oil in its compositions. Chen, on the contrary, is limited to "nicotine base and its salts." The Action, however, states that "regarding nicotine oil . . . , applicants failed to show unexpected results obtained from nicotine oil . . . over the use of nicotine salts disclosed by Chen et al." (Office Action, p. 7). As mentioned above, however, nicotine salts are not suitable for use in orally dissolvable films containing the enteric/acidic polymers of the present invention because the solubility of the enteric polymer is pH-dependent.

Applicants have recognized that the use of a neutral nicotine, such as a nicotine oil, overcomes the problems associated with the decrease in pH from the nicotine salts. There are, however, problems associated with using neutral nicotine oils in films. When neutral, nicotine oil is quite volatile and this is particularly an issue when forming nicotine-containing films using a solvent coating process. For example, during the drying process to remove solvents, much of the neutral nicotine evaporates from the film, resulting in a film containing much less nicotine than desired. In addition, the film is susceptible to additional loss of nicotine during storage. To overcome these problems, Applicants recognized the importance of partially pre-neutralizing Eudragit polymer using a neutralizing agent. The benefits are four-fold. First, the nicotine exists as a monocation at the formulated pH (6 to 6.5) which is no longer volatile. Second, the formulated pH which only partially pre-neutralizes the enteric polymer, allows the polymer to serve as a polymeric ligand to immobilize the nicotine by forming an ionic complex between the nicotine and the partially pre-neutralized enteric polymer to prevent it from escaping with solvent (water/ethanol) during the drying process. Third, the nicotine and Eudragit ionic and polymeric complex prevent the physical immigration of nicotine during storage and stability study. Fourth, the formulated pH which partially pre-neutralizes Eudragit, provides a film that keeps its integrity when handled and dissolves rapidly in a small volume of saliva.

Claims 8, 35 and 37 are rejected under 35 U.S.C. 103(a) as allegedly being obvious over the combination of Chen and Lerner as evident by Lamosa and further in view of Adusumili et al. (US 2004/0037879).

As previously asserted by Applicants in the response to office action dated April 9, 2010, Applicants submit that Adusumilli would not preclude patentability of claims 8, 35,

and 37 in view of 35 U.S.C. § 103(c). In particular, to the extent Adusumilli qualifies as prior art to the present application, it would be under 35 U.S.C. § 102(e) (Adusumilli published on February 26, 2004, after the July 24, 2003, priority date of the present application). Records indicate that both Adusumilli and the present application were under common ownership by SmithKline Beecham Corporation at the time the subject invention was made. The assignment for the present application is at Reel 017777, Frame 0420 and the assignment for Adusumilli is at Reel 013581 Frame 0852.

Accordingly, Adusumilli is not available as prior art in accordance with 35 U.S.C. § 103(c) and Applicants respectfully request withdrawal of the rejection of claims 8, 35, and 37 under 35 U.S.C. § 103(a).

Conclusion

Applicants believe that the foregoing constitutes a complete and full response to the Office Action of record. An indication of allowability of the claimed design is requested respectfully. Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned attorney at the number below.

Respectfully submitted,

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